Remarks

Claims 1-26 are pending in the subject application. By this Amendment, Applicants have amended claims 1, 3, 9, and 11 and canceled claims 17-26. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. With respect to the amendments to claims 1, 3, 9, and 11, Applicants have amended the claims to correct an inadvertent error introduced into the claims. The numeric designation set forth in the claims as previously presented refers to the internal designation of the polypeptide or polynucleotide associated with a specific SEQ ID No. Applicants inadvertently referred to this designation as a "clone". Support for the changes made to the claims can be found in the originally filed specification at page 14, lines 12-14 ("Table I provides the applicant's internal designation number assigned to each sequence identification number and indicates whether the sequence is a nucleic acid sequence or a polypeptide sequence, and in which vector the cDNA was cloned.") and at page 28, lines 2-11. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1-16 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

At the outset, Applicants gratefully acknowledge the Examiner's withdrawal of the objections to the specification and the rejections under 35 U.S.C. § 112, first paragraph.

Claims 1-26 are rejected under 35 U.S.C. § 101 as not being supported by either a specific and substantial asserted utility or a well-established utility. The claims are also rejected under 35 U.S.C. § 112, first paragraph, on the basis that one skilled in the art would not know how to use the claimed invention as there is no specific and substantial asserted utility or a well-established utility for the claimed invention. Applicants respectfully traverse.

The Office Action appears argue that the subject invention lacks patentable utility as the biological function or role of the polypeptide of SEQ ID NO: 297 has not been established, the claimed polypeptides do not have utility as a synaptogyrin protein (see Office Action at page 4, lines 11-16). Applicants respectfully submit that the fact that the specification has not established the claimed polypeptide is a functional synaptogyrin with experimental data is not sufficient to properly reject the claimed invention under 35 U.S.C. § 101. The M.P.E.P sets forth the standard for assessing the utility of an invention in § 2107.02:

> To overcome the presumption of truth that an assertion of utility by the applicant enjoys, Office personnel must establish that it is more likely than not that one of ordinary skill in the art would doubt (i.e., "question") the truth of the statement of utility. (...) The *prima facie* showing must be set forth in a well-reasoned statement. Any rejection based on lack of utility should include a detailed explanation why the claimed invention has no specific and substantial credible utility.

In view of the above, Applicants respectfully submit that there is no requirement that they must establish, or demonstrate, the function of a claimed polypeptide. Rather, the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would question the asserted utility of the claimed polypeptide.

As set forth in the Amendment dated March 22, 2006, one of skill in the art would believe that the claimed polypeptide is a synaptogyrin in view of:

- the presence of the central conserved domain (see sentence bridging pages 137-138 in Kedra *et al.* (1998));
- the strong conservation among the first 16 amino acids residues between rat; synaptogyrin and human synaptogyrin 1a and 1b (see page 138, left column, lines 6-9 of Kedra *et al.* (1998));
- a C-terminal variable end, located outside of the above-described central and N-terminal part, that is likely to convey the functional specificity of each protein (see page 138, right column, lines 2-5 of Kedra *et al.* (1998)); and
- the two cysteines present between the first and the second transmembrane domains of rat synaptogyrin that form a disulfide bond (see page 138, right column, lines 17-20 of Kedra *et al.* (1998)).

The last Office Action alleges that one of skill in the art would question the assertion that the claimed polypeptide is a synaptogyrin because:

- the claimed polypeptide is structurally different from other members of synaptogyrin family in terms of C-terminal functional domain;
- the claimed polypeptide is structurally different from other members of synaptogyrin family in terms of transmembrane helices in the central conserved region; and

- the specification has not established the claimed polypeptide is a functional synaptogyrin.

Applicants respectfully assert that the fact that the claimed polypeptide is different from other members of synaptogyrin family in terms of C-terminal functional domain does not contradict the fact that it is a synaptogyrin. Furthermore, a number of splice variants of the polypeptide are recognized to exist (see Kedra *et al.* and the attached OMIM printout) and various members of the synaptogyrin family exhibit a C-terminal sequence that is variable and is likely to convey the functional specificity of each protein (see page 138, right column, lines 2-5 of Kedra *et al.* (1998)).

Applicants further assert that the fact that the claimed polypeptide is different from other members of synaptogyrin family in terms of transmembrane helices in the central conserved region would not lead one of skill in the art to question the assertion that the claimed polypeptide is a synaptogyrin. As shown in Appendix 1 of the Amendment dated March 22, 2006, the known members of the synaptogyrin family do not exhibit a conserved number of transmembrane helices in the central conserved region. Therefore, one of skill in the art would not draw any conclusion based on the variable number of transmembrane helices.

In view of the foregoing arguments, Applicants respectfully submit that the Patent Office has failed to meet its burden establishing that the claimed invention lacks a specific and/or a substantial credible utility and that one skilled in the art would have accepted the asserted utility of the claimed invention and known how to use the claimed invention in view of the teachings of the as-filed specification. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-3, 5, 7, 9-11, 13, 15, and 17-26 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully assert that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan that they had possession of the claimed invention. The instant Office Action indicates that claim 1 is directed to polypeptides in which up to 5% of the amino acid residues in SEQ ID NO: 297 may be inserted, deleted or substituted with another amino acid. The Action further asserts that, since the specification does not identify the amino acid residues that are essential to the function of the

polypeptide, one of skill in the art would not know how to identify a functional polypeptide. As noted above, Applicants have canceled claims 17-26, thereby rendering the rejection of those claims moot. In a sincere effort to expedite prosecution of the subject application to completion, Applicants have amended also claims 1 and 9 to address this issue. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

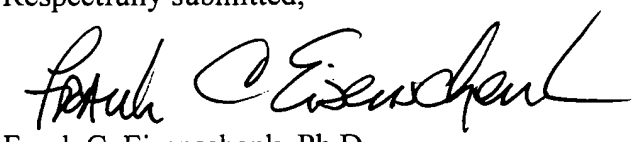
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Links

SYNAPTOGYRIN 1; SYNGR1

Gene map locus 22q13

TEXT

CLONING

Rat synaptogyrin, or RATSYNGR1, is an integral membrane protein associated with presynaptic vesicles in neuronal cells. See SYNGR2 (603926). As part of an effort to sequence the long arm of human chromosome 22, Kedra et al. (1998) identified the human homolog of RATSYNGR1, synaptogyrin-1 (SYNGR1). By a combination of EST database searching and library screening, the authors isolated cDNAs corresponding to 3 alternatively spliced transcripts, which they designated SYNGR1a-c. The predicted 1a, 1b, and 1c proteins contain 234, 191, and 192 amino acids, respectively. Northern blot analysis revealed that the 4.5-kb SYNGR1a mRNA is expressed at high levels in brain. The other transcript forms are expressed at low levels in nonneuronal tissues. In situ hybridization to embryonic and adult mouse tissues confirmed that SYNGR1a, the most abundant transcript form, shows predominantly neuronal expression. Kedra et al. (1998) also identified cDNAs encoding the related human proteins SYNGR2 and SYNGR3 (603927) and mouse Syngr1b. Like RATSYNGR1, the mouse and human synaptogyrin family members contain 4 membrane-spanning domains. The conserved central portion of SYNGR1a shares 54%, 61%, and 92% identity with that of SYNGR2, SYNGR3, and RATSYNGR1, respectively.

GENE STRUCTURE

Kedra et al. (1998) determined that the SYNGR1 gene contains 6 exons.

MAPPING

By inclusion within mapped clones, Kedra et al. (1998) mapped the SYNGR1 gene to chromosome 22q13. These authors found that SYNGR2 is located on 17qter and noted that the synaptogyrins and several other gene families contain paralogous genes located on chromosomes 17 and 22. They stated that this result supports the hypothesis that 17q and 22q are evolutionarily closely related, and that these 2 regions in the human genome are the result of a large chromosome duplication.

ANIMAL MODEL

Using gene targeting, Janz et al. (1999) generated mice lacking Syngr1. They bred these Syngr1 knockout mice against Syp (313475) knockout mice generated by McMahon et al. (1996) to create double knockout mice deficient in both Syp and Syngr1. Both single and double knockout mice were viable and fertile. Morphologic and biochemical analysis showed that the architecture and composition of synapses were unaltered in the brains of Syngr1 single knockout and Syngr1/Syp double knockout mutant mice. Electrophysiologic recordings in the hippocampal CA1 region revealed that

short- and long-term synaptic plasticity was severely reduced in the Syngr1/Syp double knockout mice without changes in the fundamental release apparatus, vesicle cycling, or release probability. Janz et al. (1999) concluded that Syngr1 and Syp perform essential and redundant functions in synaptic plasticity without being required for synaptic transmission as such.

From the results of cotransfection experiments, Janz et al. (1999) concluded that Syp and Syngr1 are phosphorylated by c-fyn and c-src tyrosine kinases. The absence of Syp and Syngr1 in knockout mice did not markedly affect tyrosine phosphorylation of other proteins.

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